# Changes in 4-Year Antimicrobial Resistance Pattern of Gram-Positive Bacteria at the Main Referral Teaching Hospital, Tehran, Iran

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**Abstract-** Infectious diseases are one of the most common causes of morbidity and mortality and the spread of resistant microorganisms is playing a significant role in this regard. The purpose of this study was to assess the trend in antimicrobial resistance of gram-positive bacteria at the main referral teaching hospital in Tehran during a 4-year period. All patients' biological isolates such as blood, urine, wound drainage, synovial fluid, sputum, and cerebrospinal fluid sent to the central laboratory of the hospital from 2007 to 2010 for identification and subsequently, antimicrobial susceptibility testing by Kirby-Bauer disc diffusion method were considered. All isolates (100%) of *S. aureus* were sensitive to vancomycin and linezolid and resistant to amoxicillin. The rate of *S. aureus* resistance to oxacillin increased from 60.78% in 2007 to 72% in 2010. All isolates of Streptococci in 2007 and 2008 were sensitive to vancomycin; while, 3.33% and 4.76% of Streptococci isolates were reported to be vancomycin-resistant in 2009 and 2010, respectively. Enterococci isolated from the entire specimens were identified to be sensitive to teicoplanin and linezolid and resistant to cloxacillin and oxacillin. The rates of Enterococci sensitivity to vancomycin were 90.91%, 81.25%, 86.67%, and 93.3% in 2007, 2008, 2009, and 2010, respectively. Changes of antibiotics sensitivity against g positive pathogens were significant during four years in this study. To minimize the spread of resistant gram positive pathogens, periodic and regular surveillance of antimicrobial resistance pattern is highly recommended.

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**Keywords:** G positive bacteria; Antibiotic; Resistance

## Introduction

Infectious diseases are one of the most common causes of morbidity and mortality worldwide (1). Among pathogens, gram-positive bacteria are responsible for a large number of community-acquired and health-care-associated infections at different sites including bone and joint, upper and lower respiratory tract, bloodstream, central nervous system, urinary tract, and skin and soft tissue. Among gram-positive pathogens, *Staphylococcus aureus*, *Streptococcus pneumoniae*, and more recently, enterococci are the most prevalent and as a subject of clinical interest (2).

The constant increase in antimicrobial resistance among pathogens represents a major global public health concern and adds to the cost of health care (3). Over the counter availability, indiscriminate, and inappropriate use of antimicrobial agents contribute significantly in the development of antibiotic-resistant bacteria (4). It has been shown that up to 50% of prescribing antimicrobial agents in hospitals may be inappropriate (5). Therefore, information on the most probable causative bacteria and their resistance patterns could help clinicians in selecting an optimized (effective and safe) antimicrobial agent for empirical therapy, develop rational prescription guidelines, and make policy decisions.

Despite performing numerous regional or national surveillance studies on epidemiology, microbiology, and antimicrobial resistance pattern of bacteria (in Iran), the trend of resistance to several antimicrobials over a certain period of time has not been considered much.

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The aim of the present study was to assess the trend in antimicrobial resistance of gram-positive bacteria during a 4-year period at an infectious diseases ward in Iran.

## Materials and Methods

A retrospective study was performed on laboratory records of patients during a 4-year period from 2007 to 2010 hospitalized at 60-bed infectious diseases ward of Imam Khomeini Hospital, a multispecialty healthcare university setting affiliated to Tehran University of Medical Sciences. The Institutional Review Board (IRB) and the Medical Ethics Committee of the hospital approved the study.

All patient biological isolates such as blood, urine, sputum, wound drainage, abscess, synovial, pleural, ascitic, and cerebrospinal fluid were sent to the central laboratory of the hospital. Samples were taken aseptically from suspected patients before starting empirical antibiotic therapy as well as during maintenance antibiotic treatment for evaluating microbiological response. Identification of microorganisms from collected samples was performed by gram staining and standard biochemical tests including catalase, coagulase, DNase, bile esculin hydrolysis, growth on sodium chloride, susceptibility to optochin, colonial morphology and hemolysis. Antimicrobial susceptibility was determined by Kirby-Bauer disc diffusion method using Diagnostic Sensitivity Test (DST) agar. The diameter of the inhibition zone was a function of susceptibility of the microorganism. Based on the size of inhibition zone, the isolated microorganism was determined to be resistant, intermediately resistant, or sensitive to the certain antimicrobial agent. Antibiotic sensitivity discs (Himedia Laboratories, Mumbai, India) used for testing antibiotic susceptibilities were as follows:

Penicilin G (10 mcg/disc), oxacillin (5 mcg/disc), erythromycin (5 mcg/disc), clindamycin (2 mcg/disc), cephalothin (30 mcg/disc) or cephazolin (30 mcg/disc), trimethoprim/sulfamethoxazole [25 (1.25/23.75) mcg/disc], gentamicin (10 mcg/disc), chloramphenicol (30 mcg/disc), rifampin (5 mcg/disc), and vancomycin (30 mcg/disc) for *Staphylococcus*; ampicillin (10 mcg/disc), erythromycin (5 mcg/disc), chloramphenicol (30 mcg/disc), clindamycin (2 mcg/disc), vancomycin (30 mcg/disc), ceftriaxone (30 mcg/disc), and ciprofloxacin (5 mcg/disc) for *Streptococcus* and ampicillin (10 mcg/disc), erythromycin (5 mcg/disc), chloramphenicol (30 mcg/disc), ciprofloxacin (5 mcg/disc), rifampin (5 mcg/disc), ceftriaxone (30 mcg/disc), gentamicin (10 mcg/disc) or amikacin (30 mcg/disc), nitrofurantoin (300 mcg/disc), and linezolid (30 mcg/disc) for *Enterococci*.

### Statistical analysis

Categorical variables were expressed as percentage. Statistical Package for the Social Sciences (SPSS) version 11.5 (SPSS Inc., Chicago, IL, USA) was used for descriptive statistical analysis.

## Results

During a 4-year period, 1745 positive biological specimens sent to the central laboratory of the hospital. Blood (46.2%), urine (27%), and wound drainage (13.7%) were the most frequent positive specimen sources. Five hundred and twelve (29.34%) isolates were identified as gram-positive bacteria. Table 1 list the frequency of detected gram-positive bacteria in different biological specimens. *Staphylococcus aureus* (36.72%), *Staphylococcus epidermidis* (23.63%), and Streptococci (18.16%) were the most common isolated gram-positive bacteria from all samples. The most frequent gram-positive bacteria isolated from blood and urine specimens were *S. aureus* (7.19%) and Streptococci (3.39%), respectively. *S. aureus* was also the most common isolated gram-positive bacteria from wound drainage (28.57%) and other samples (26.2%).

**Table 1.** Frequency of detected gram-positive bacteria in different biological specimens (n=512).

| Microorganism | Blood n (%) | Urine n (%) | Wound drainage n (%) | Other† n (%) |
|---|---|---|---|---|
| *Staphylococcus aureus* | 58 | 2 | 68 | 60 |
| *Staphylococcus epidermidis* | 81 | 15 | 10 | 15 |
| Streptococci | 42 | 16 | 18 | 17 |
| Enterococcus | 21 | 5 | 23 | 11 |
| *Corynebacterium sp.* | 19 | 0 | 1 | 0 |
| *Bacillus sp.* | 13 | 0 | 0 | 1 |
| *Micrococcus sp.* | 5 | 0 | 0 | 0 |

† Including sputum, abscess, synovial, pleural, ascitic, and cerebrospinal fluid.

The 4-year antimicrobial resistance trend of gram-positive bacteria to different antimicrobials is demonstrated in tables 2 and 3. The highest resistance rates (36.47% to 65.62%) were seen with Enterococcus sp. followed by *S. epidermidis* (31.28% to 45.37%). Among detected gram positives, *S. aureus* was the most susceptible pathogen with resistance rates of 24.52% to 41.63%. The most frequent resistance during the study period was observed with penicillin G (73.63% to 80.25%), oxacillin (57.45% to 73.5%), and amoxicillin (33.33% to 80.95%). Linezolid, teicoplanin, and vancomycin were the most active antimicrobial agents against gram positive bacteria with resistance rates of 0%, 0%, and 1.09% to 3.28%, respectively.

**Table 2.** The 4-year antimicrobial resistance trend of gram-positive bacteria to different antimicrobials.

| Antimicrobial agent/ microorganism | Susceptibility | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sensitive; n (%) | | | | Intermediate; n (%) | | | | Resistant; n (%) | | | |
| | 2007 | 2008 | 2009 | 2010 | 2007 | 2008 | 2009 | 2010 | 2007 | 2008 | 2009 | 2010 |
| Trimethoprim/ Sulfamethoxazole | | | | | | | | | | | | |
| *Enterococcus sp.* | 8 | 12 | 9 | 24 | 0 | 0 | 0 | 0 | 28 | 48 | 12 | 24 |
| *S. aureus* | 96 | 107 | 103 | 49 | 6 | 0 | 3 | 0 | 48 | 32 | 36 | 30 |
| *S. epidermidis* | 24 | 52 | 45 | 28 | 8 | 0 | 0 | 0 | 40 | 65 | 36 | 44 |
| *Streptococcus sp.* | 12 | 20 | 28 | 16 | 0 | 0 | 0 | 0 | 21 | 40 | 54 | 40 |
| Total | 140 | 191 | 185 | 117 | 14 | 0 | 3 | 0 | 137 | 185 | 138 | 138 |
| | (48.1) | (50.79) | (56.75) | (45.88) | (4.8) | (0) | (0.92) | (0) | (47.08) | (49.2) | (42.33) | (54.12) |
| Cephalotin | | | | | | | | | | | | |
| *Enterococcus sp.* | 1 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 1 | 3 | 0 | 0 |
| *S. aureus* | 39 | 42 | 49 | 30 | 1 | 0 | 0 | 0 | 27 | 6 | 29 | 21 |
| *S. epidermidis* | 14 | 46 | 9 | 37 | 0 | 0 | 0 | 3 | 3 | 15 | 0 | 0 |
| *Streptococcus sp.* | 3 | 28 | 24 | 8 | 6 | 0 | 0 | 0 | 9 | 12 | 4 | 4 |
| Total | 57 | 116 | 82 | 79 | 7 | 0 | 0 | 3 | 40 | 36 | 33 | 25 |
| | (54.81) | (76.32) | (71.3) | (73.83) | (6.73) | (0) | (0) | (2.8) | (38.46) | (23.68) | (28.69) | (23.36) |
| Rifampin | | | | | | | | | | | | |
| *Enterococcus sp.* | 0 | 4 | 18 | 12 | 0 | 0 | 0 | 0 | 0 | 8 | 9 | 12 |
| *S. aureus* | 0 | 4 | 103 | 42 | 0 | 0 | 0 | 0 | 0 | 4 | 18 | 15 |
| *S. epidermidis* | 0 | 0 | 54 | 51 | 0 | 0 | 0 | 0 | 0 | 0 | 12 | 12 |
| *Streptococcus sp.* | 3 | 13 | 56 | 40 | 0 | 0 | 0 | 0 | 0 | 0 | 13 | 28 |
| Total | 3 | 21 | 231 | 145 | 0 | 0 | 0 | 0 | 0 | 12 | 52 | 67 |
| | (100) | (63.64) | (81.63) | (68.39) | (0) | (0) | (0) | (0) | (0) | (36.36) | (18.37) | (31.6) |
| Amikacin | | | | | | | | | | | | |
| *Enterococcus sp.* | 12 | 16 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 8 | 0 | 4 |
| *S. aureus* | 30 | 41 | 3 | 0 | 6 | 0 | 0 | 0 | 12 | 16 | 0 | 0 |
| *S. epidermidis* | 44 | 40 | 9 | 4 | 4 | 0 | 0 | 0 | 12 | 4 | 6 | 3 |
| *Streptococcus sp.* | 18 | 24 | 0 | 4 | 0 | 0 | 0 | 0 | 9 | 0 | 4 | 0 |
| Total | 104 | 121 | 12 | 8 | 10 | 0 | 0 | 0 | 41 | 28 | 10 | 7 |
| | (67.09) | (81.21) | (54.55) | (53.33) | (6.45) | (0) | (0) | (0) | (26.45) | (18.79) | (45.45) | (46.67) |
| Ampicillin/Sulbactam | | | | | | | | | | | | |
| *Enterococcus sp.* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *S. aureus* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *S. epidermidis* | 0 | 4 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *Streptococcus sp.* | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 |
| Total | 0 | 4 | 3 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 4 |
| | (0) | (100) | (60) | (50) | (0) | (0) | (0) | (0) | (0) | (0) | (40) | (50) |
| Cefazolin | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Enterococcus sp.* | 0 | 8 | 15 | 0 | 0 | 0 | 0 | 0 | 0 | 24 | 0 | 4 |
| *S. aureus* | 48 | 114 | 9 | 3 | 0 | 0 | 0 | 0 | 27 | 40 | 6 | 6 |
| *S. epidermidis* | 20 | 84 | 9 | 4 | 0 | 4 | 0 | 0 | 24 | 8 | 0 | 0 |
| *Streptococcus sp.* | 3 | 16 | 8 | 4 | 0 | 0 | 0 | 0 | 3 | 20 | 8 | 0 |
| Total | 71 | 222 | 41 | 11 | 0 | 5 | 0 | 0 | 54 | 92 | 14 | 10 |
| | (56.8) | (69.59) | (74.55) | (52.38) | (0) | (1.57) | (0) | (0) | (43.2) | (28.84) | (25.45) | (47.62) |
| Ciprofloxacin | | | | | | | | | | | | |
| *Enterococcus sp.* | 12 | 8 | 18 | 24 | 0 | 0 | 0 | 0 | 12 | 33 | 15 | 12 |
| *S. aureus* | 78 | 46 | 99 | 40 | 3 | 4 | 0 | 6 | 3 | 0 | 68 | 33 |
| *S. epidermidis* | 20 | 32 | 45 | 28 | 4 | 0 | 0 | 0 | 28 | 8 | 24 | 46 |
| *Streptococcus sp.* | 21 | 28 | 52 | 48 | 3 | 0 | 0 | 0 | 6 | 20 | 32 | 24 |
| Total | 131 | 114 | 214 | 140 | 10 | 4 | 0 | 6 | 49 | 61 | 139 | 115 |
| | (68.95) | (63.69) | (60.62) | (53.64) | (5.26) | (2.23) | (0) | (2.29) | (25.79) | (34.08) | (39.38) | (44.06) |
| Clindamycin | | | | | | | | | | | | |
| *Enterococcus sp.* | 0 | 0 | 3 | 20 | 0 | 0 | 0 | 0 | 8 | 28 | 21 | 32 |
| *S. aureus* | 93 | 109 | 70 | 44 | 0 | 0 | 0 | 0 | 63 | 41 | 57 | 45 |
| *S. epidermidis* | 24 | 80 | 36 | 36 | 0 | 0 | 0 | 0 | 64 | 32 | 33 | 44 |
| *Streptococcus sp.* | 18 | 16 | 36 | 40 | 0 | 0 | 0 | 0 | 12 | 44 | 60 | 32 |
| Total | 135 | 205 | 145 | 140 | 0 | 0 | 0 | 0 | 147 | 145 | 171 | 153 |
| | (47.87) | (58.57) | (45.89) | (47.78) | (0) | (0) | (0) | (0) | (52.13) | (41.43) | (54.11) | (52.22) |
| Cloxacillin | | | | | | | | | | | | |
| *Enterococcus sp.* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 0 | 0 | 0 |
| *S. aureus* | 15 | 18 | 0 | 0 | 0 | 4 | 0 | 0 | 6 | 16 | 0 | 0 |
| *S. epidermidis* | 12 | 16 | 0 | 4 | 0 | 0 | 0 | 0 | 20 | 20 | 0 | 0 |
| *Streptococcus sp.* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 8 | 0 | 0 |
| Total | 27 | 34 | 0 | 4 | 0 | 4 | 0 | 0 | 37 | 44 | 0 | 0 |
| | (42.19) | (41.46) | (0) | (100) | (0) | (4.88) | (0) | (0) | (57.81) | (53.66) | (0) | (0) |
| Imipenem | | | | | | | | | | | | |
| *Enterococcus sp.* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *S. aureus* | 0 | 4 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 11 | 0 |
| *S. epidermidis* | 0 | 0 | 12 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| *Streptococcus sp.* | 3 | 0 | 12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 3 | 4 | 33 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 11 | 0 |
| | (42.86) | (100) | (75) | (0) | (0) | (0) | (0) | (0) | (57.14) | (0) | (25) | (0) |
| Linezolid | | | | | | | | | | | | |
| *Enterococcus sp.* | 0 | 8 | 30 | 28 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *S. aureus* | 0 | 0 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *S. epidermidis* | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *Streptococcus sp.* | 0 | 0 | 42 | 32 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 0 | 8 | 75 | 67 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | (0) | (100) | (100) | (100) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| Oxacillin | | | | | | | | | | | | |
| *Enterococcus sp.* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 16 | 9 | 8 |
| *S. aureus* | 57 | 80 | 67 | 21 | 3 | 0 | 0 | 0 | 93 | 40 | 73 | 54 |
| *S. epidermidis* | 28 | 28 | 21 | 28 | 0 | 0 | 0 | 0 | 52 | 66 | 51 | 49 |
| *Streptococcus sp.* | 6 | 8 | 16 | 4 | 0 | 4 | 0 | 0 | 18 | 40 | 48 | 36 |
| Total | 91 | 116 | 104 | 53 | 3 | 4 | 0 | 0 | 167 | 162 | 181 | 147 |
| | (34.87) | (41.13) | (36.49) | (26.5) | (1.15) | (1.42) | (0) | (0) | (63.98) | (57.45) | (63.51) | (73.5) |
| Penicillin G | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Enterococcus sp.* | 8 | 4 | 3 | 8 | 0 | 0 | 0 | 0 | 12 | 44 | 9 | 16 |
| *S. aureus* | 18 | 42 | 9 | 0 | 0 | 0 | 0 | 0 | 93 | 73 | 33 | 18 |
| *S. epidermidis* | 16 | 20 | 3 | 9 | 0 | 0 | 0 | 0 | 36 | 60 | 48 | 30 |
| *Streptococcus sp.* | 3 | 16 | 17 | 12 | 0 | 0 | 0 | 0 | 18 | 52 | 40 | 20 |
| Total | 45 | 82 | 32 | 29 | 0 | 0 | 0 | 0 | 159 | 229 | 130 | 84 |
| | (22.06) | (26.37) | (19.75) | (25.66) | (0) | (0) | (0) | (0) | (77.94) | (73.63) | (80.25) | (74.34) |
| Ceftriaxone | | | | | | | | | | | | |
| *Enterococcus* | 0 | 4 | 3 | 0 | 0 | 0 | 0 | 0 | 8 | 0 | 0 | 4 |
| *S. aureus* | 0 | 0 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 3 |
| *S. epidermidis* | 0 | 0 | 3 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *Streptococcus* | 3 | 4 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 0 |
| Total | 3 | 8 | 9 | 11 | 0 | 0 | 0 | 0 | 8 | 0 | 9 | 7 |
| | (27.27) | (100) | (50) | (61.11) | (0) | (0) | (0) | (0) | (72.73) | (0) | (50) | (38.89) |
| Vancomycin | | | | | | | | | | | | |
| *Enterococcus sp.* | 40 | 52 | 39 | 42 | 0 | 0 | 0 | 0 | 4 | 12 | 6 | 3 |
| *S. aureus* | 175 | 175 | 165 | 89 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 3 |
| *S. epidermidis* | 104 | 145 | 87 | 84 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *Streptococcus sp.* | 45 | 84 | 116 | 80 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 4 |
| Total | 364 | 456 | 407 | 295 | 0 | 0 | 0 | 0 | 4 | 12 | 13 | 10 |
| | (98.91) | (97.44) | (96.9) | (96.72) | (0) | (0) | (0) | (0) | (1.09) | (2.56) | (3.09) | (3.28) |
| Amoxicillin | | | | | | | | | | | | |
| *Enterococcus sp.* | 24 | 4 | 0 | 4 | 0 | 0 | 0 | 0 | 20 | 4 | 0 | 8 |
| *S. aureus* | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 0 | 3 |
| *S. epidermidis* | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *Streptococcus sp.* | 12 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 4 | 0 | 0 |
| Total | 40 | 4 | 0 | 4 | 0 | 0 | 0 | 4 | 20 | 17 | 0 | 11 |
| | (66.67) | (19.05) | (0) | (21.05) | (0) | (0) | (0) | (21.05) | (33.33) | (80.95) | (0) | (57.89) |
| Teicoplanin | | | | | | | | | | | | |
| *Enterococcus sp.* | 0 | 0 | 6 | 8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *S. aureus* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *S. epidermidis* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *Streptococcus sp.* | 0 | 0 | 16 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 0 | 0 | 22 | 12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | (0) | (0) | (100) | (100) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| Gentamicin | | | | | | | | | | | | |
| *Enterococcus sp.* | 12 | 12 | 6 | 4 | 0 | 4 | 0 | 0 | 4 | 24 | 3 | 8 |
| *S. aureus* | 48 | 132 | 84 | 38 | 6 | 0 | 0 | 3 | 18 | 24 | 48 | 30 |
| *S. epidermidis* | 20 | 84 | 54 | 44 | 4 | 8 | 0 | 0 | 20 | 16 | 21 | 16 |
| *Streptococcus sp.* | 12 | 48 | 44 | 12 | 0 | 0 | 0 | 4 | 3 | 12 | 28 | 24 |
| Total | 92 | 276 | 188 | 98 | 10 | 12 | 0 | 7 | 45 | 76 | 100 | 78 |
| | (62.59) | (75.82) | (65.28) | (53.55) | (6.8) | (3.29) | (0) | (3.83) | (30.6) | (20.88) | (34.72) | (42.62) |
| Ampicillin | | | | | | | | | | | | |
| *Enterococcus sp.* | 16 | 28 | 21 | 32 | 0 | 0 | 0 | 0 | 16 | 33 | 9 | 4 |
| *S. aureus* | 0 | 20 | 6 | 3 | 0 | 0 | 0 | 0 | 0 | 4 | 6 | 0 |
| *S. epidermidis* | 0 | 12 | 9 | 9 | 0 | 0 | 0 | 0 | 0 | 8 | 3 | 0 |
| *Streptococcus sp.* | 9 | 16 | 16 | 36 | 0 | 0 | 0 | 0 | 0 | 8 | 8 | 0 |
| Total | 25 | 76 | 52 | 80 | 0 | 0 | 0 | 0 | 16 | 53 | 26 | 4 |
| | (60.98) | (58.91) | (66.67) | (95.24) | (0) | (0) | (0) | (0) | (39.02) | (41.09) | (33.33) | (4.76) |

**Table 3.** The 4-year antimicrobial resistance trend of gram-positive bacteria to different antimicrobials.

| Microorganism/ Antimicrobial agent | Susceptibility | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sensitive; n (%) | | | | Intermediate; n (%) | | | | Resistant; n (%) | | | |
| | 2007 | 2008 | 2009 | 2010 | 2007 | 2008 | 2009 | 2010 | 2007 | 2008 | 2009 | 2010 |
| *Enterococcus sp.* | | | | | | | | | | | | |
| Amikacin | 12 | 16 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 8 | 0 | 4 |
| Amoxicillin | 24 | 4 | 0 | 4 | 0 | 0 | 0 | 0 | 20 | 4 | 0 | 8 |
| Ampicillin | 12 | 21 | 14 | 24 | 0 | 0 | 0 | 0 | 16 | 32 | 9 | 4 |
| Ampicillin/Sulbactam | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Ceftriaxone | 0 | 4 | 3 | 0 | 0 | 0 | 0 | 0 | 8 | 0 | 0 | 4 |
| Cephalotin | 4 | 0 | 0 | 8 | 0 | 0 | 0 | 0 | 4 | 12 | 0 | 0 |
| Cephazolin | 0 | 6 | 15 | 0 | 0 | 0 | 0 | 0 | 0 | 24 | 0 | 4 |
| Ciprofloxacin | 9 | 6 | 18 | 18 | 0 | 0 | 0 | 0 | 12 | 32 | 15 | 12 |
| Clindamycin | 0 | 0 | 3 | 20 | 0 | 0 | 0 | 0 | 8 | 28 | 21 | 32 |
| Cloxacillin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 0 | 0 | 0 |
| Gentamicin | 12 | 12 | 6 | 4 | 0 | 4 | 0 | 0 | 4 | 24 | 3 | 8 |
| Linezolid | 0 | 8 | 30 | 28 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Oxacillin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 16 | 9 | 8 |
| Penicillin G | 8 | 4 | 3 | 8 | 0 | 0 | 0 | 0 | 12 | 44 | 9 | 16 |
| Rifampin | 0 | 4 | 16 | 12 | 0 | 0 | 0 | 0 | 0 | 8 | 9 | 12 |
| Teicoplanin | 0 | 0 | 6 | 8 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Trimethoprim/ Sulfamethoxazole | 8 | 12 | 9 | 24 | 0 | 0 | 0 | 0 | 28 | 48 | 12 | 24 |
| Vancomycin | 40 | 52 | 39 | 56 | 0 | 0 | 0 | 0 | 4 | 12 | 6 | 4 |
| Total | 129 | 149 | 162 | 214 | 0 | 4 | 0 | 0 | 136 | 292 | 93 | 140 |
| | (48.68) | (33.48) | (64.71) | (60.45) | (0) | (0.89) | (0) | (0) | (51.32) | (65.62) | (36.47) | (39.55) |
| *Staphylococcus aureus* | | | | | | | | | | | | |
| Amikacin | 30 | 40 | 3 | 0 | 6 | 0 | 0 | 0 | 12 | 16 | 0 | 0 |
| Amoxicillin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 0 | 3 |
| Ampicillin | 0 | 20 | 6 | 3 | 0 | 0 | 0 | 0 | 0 | 4 | 6 | 0 |
| Ampicillin/Sulbactam | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Ceftriaxone | 0 | 0 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 3 |
| Cephalotin | 39 | 56 | 48 | 30 | 3 | 0 | 0 | 0 | 27 | 8 | 27 | 21 |
| Cephazolin | 48 | 112 | 9 | 3 | 0 | 0 | 0 | 0 | 27 | 40 | 6 | 6 |
| Ciprofloxacin | 78 | 44 | 99 | 39 | 3 | 4 | 0 | 6 | 3 | 0 | 66 | 33 |
| Clindamycin | 93 | 108 | 69 | 42 | 0 | 0 | 0 | 0 | 63 | 40 | 57 | 45 |
| Cloxacillin | 15 | 16 | 0 | 0 | 0 | 4 | 0 | 0 | 6 | 16 | 0 | 0 |
| Gentamicin | 48 | 128 | 81 | 36 | 6 | 0 | 0 | 3 | 18 | 24 | 48 | 30 |
| Imipenem | 0 | 4 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 0 |
| Linezolid | 0 | 0 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Oxacillin | 57 | 80 | 66 | 21 | 2 | 0 | 0 | 0 | 93 | 40 | 72 | 54 |
| Penicillin G | 18 | 40 | 9 | 0 | 0 | 0 | 0 | 0 | 93 | 72 | 33 | 18 |
| Rifampin | 0 | 4 | 102 | 42 | 0 | 0 | 0 | 0 | 0 | 4 | 18 | 15 |
| Trimethoprim/Sulfamethoxazole | 96 | 104 | 102 | 48 | 6 | 0 | 3 | 0 | 48 | 32 | 36 | 30 |
| Vancomycin | 174 | 172 | 162 | 87 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 3 |
| Total | 696 | 928 | 771 | 357 | 26 | 8 | 3 | 9 | 390 | 304 | 384 | 261 |
| | (62.59) | (74.84) | (66.58) | (56.94) | (2.34) | (0.65) | (0.26) | (1.44) | (35.07) | (24.52) | (33.16) | (41.63) |
| *Staphylococcus epidermidis* | | | | | | | | | | | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Amikacin | 44 | 40 | 9 | 4 | 6 | 0 | 0 | 0 | 12 | 4 | 3 | 4 |
| Amoxicillin | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Ampicillin/Sulbactam | 0 | 4 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Ampicillin | 0 | 12 | 9 | 8 | 0 | 0 | 0 | 0 | 0 | 8 | 3 | 0 |
| Ceftriaxone | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cephalotin | 28 | 60 | 9 | 40 | 0 | 0 | 0 | 4 | 4 | 20 | 0 | 0 |
| Cephazolin | 20 | 84 | 9 | 4 | 0 | 4 | 0 | 0 | 24 | 8 | 0 | 0 |
| Ciprofloxacin | 20 | 32 | 45 | 28 | 4 | 0 | 0 | 0 | 28 | 8 | 24 | 44 |
| Clindamycin | 24 | 80 | 36 | 36 | 0 | 0 | 0 | 0 | 64 | 32 | 33 | 44 |
| Cloxacillin | 12 | 16 | 0 | 4 | 0 | 0 | 0 | 0 | 20 | 20 | 0 | 0 |
| Gentamicin | 20 | 84 | 54 | 44 | 4 | 8 | 0 | 0 | 20 | 16 | 21 | 16 |
| Imipenem | 0 | 0 | 12 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| Linezolid | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Oxacillin | 28 | 28 | 21 | 28 | 0 | 0 | 0 | 0 | 52 | 64 | 51 | 48 |
| Penicillin G | 16 | 20 | 3 | 8 | 0 | 0 | 0 | 0 | 36 | 60 | 48 | 28 |
| Rifampin | 0 | 0 | 54 | 48 | 0 | 0 | 0 | 0 | 0 | 0 | 12 | 12 |
| Trimethoprim/ Sulfamethoxazole | 24 | 52 | 45 | 28 | 8 | 0 | 0 | 0 | 40 | 64 | 36 | 44 |
| Vancomycin | 104 | 144 | 87 | 84 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 344 | 656 | 396 | 368 | 22 | 12 | 0 | 4 | 304 | 304 | 231 | 240 |
| | (51.34) | (67.49) | (63.16) | (60.13) | (3.28) | (1.23) | (0) | (0.65) | (45.37) | (31.28) | (36.84) | (39.22) |
| *Streptococcus sp.* | | | | | | | | | | | | |
| Amikacin | 18 | 24 | 0 | 4 | 0 | 0 | 0 | 0 | 9 | 0 | 4 | 0 |
| Amoxicillin | 12 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 4 | 0 | 0 |
| Ampicillin/Sulbactam | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 |
| Ampicillin | 9 | 16 | 16 | 36 | 0 | 0 | 0 | 0 | 0 | 8 | 8 | 0 |
| Ceftriaxone | 3 | 4 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 |
| Cephalotin | 3 | 28 | 24 | 8 | 6 | 0 | 0 | 0 | 9 | 12 | 4 | 4 |
| Cephazolin | 3 | 16 | 8 | 4 | 0 | 0 | 0 | 0 | 3 | 20 | 8 | 0 |
| Ciprofloxacin | 21 | 28 | 52 | 48 | 3 | 0 | 0 | 0 | 6 | 20 | 32 | 24 |
| Clindamycin | 18 | 16 | 36 | 40 | 0 | 0 | 0 | 0 | 12 | 44 | 60 | 32 |
| Cloxacillin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 8 | 0 | 0 |
| Erythromycin | 9 | 28 | 56 | 44 | 3 | 8 | 0 | 0 | 15 | 36 | 60 | 40 |
| Gentamicin | 12 | 48 | 44 | 12 | 0 | 0 | 0 | 4 | 3 | 12 | 28 | 24 |
| Imipenem | 3 | 0 | 12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Linezolid | 0 | 0 | 40 | 32 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Oxacillin | 6 | 8 | 16 | 4 | 0 | 4 | 0 | 0 | 18 | 40 | 48 | 36 |
| Penicillin G | 3 | 16 | 16 | 12 | 0 | 0 | 0 | 0 | 18 | 52 | 40 | 20 |
| Rifampin | 3 | 12 | 56 | 40 | 0 | 0 | 0 | 0 | 0 | 0 | 12 | 28 |
| Teicoplanin | 0 | 0 | 16 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Trimethoprim/ Sulfamethoxazole | 12 | 20 | 28 | 16 | 0 | 0 | 0 | 0 | 21 | 40 | 52 | 40 |
| Vancomycin | 45 | 84 | 116 | 80 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 4 |
| Total | 180 | 348 | 536 | 392 | 12 | 12 | 0 | 8 | 117 | 296 | 364 | 256 |
| | (58.25) | (53.05) | (59.56) | (59.76) | (3.88) | (1.83) | (0) | (1.22) | (5.5) | (45.12) | (40.44) | (39.02) |

All isolates (100%) of *S. aureus* were sensitive to linezolid and resistant to amoxicillin. Approximately, 84% of *S. aureus* in were resistant to penicillin G in 2007; this rate reached 100% in 2010. The rate of *S. aureus* resistance to oxacillin increased from 60.78% in 2007 to 72% in 2010. All isolated *S. aureus* were susceptible to vancomycin in 2007 and 2008; while, 1.82% and 3.33% of detected *S. aureus* in 2009 and

2010 were reported to be vancomycin-resistant. *S. aureus* resistance rates to trimethoprim/ sulfamethoxazole were 36%, 23.53%, 27.66%, and 38.46% in 2007, 2008, 2009, and 2010, respectively. The resistance rate of *S. aureus* to rifampin increased from 15% in 2009 to 26.32% in 2010. The combined cephalotin and cephazolin resistant rate of *S. aureus* specimens in 2007, 2008, 2009, and 2010 were 37.5%, 22.22%, 36.67%, and 45%, respectively. All isolates of *S. epidermidis* during the study period were sensitive to vancomycin. *S. epidermidis* resistance rates to oxacillin in 2007, 2008, 2009, and 2010 were reported to be 69.23%, 75%, 94.12%, and 77.78%, respectively.

All isolates of Streptococci in 2007 and 2008 were sensitive to vancomycin; while, 3.33% and 4.76% of isolated Streptococci were reported to be vancomycin-resistant in 2009 and 2010, respectively. The penicillin G resistant rate of Streptococci specimen in 2007, 2008, 2009, and 2010 were 85.71%, 76.47%, 71.43%, and 62.5%, respectively. The whole Streptococci isolates in 2007, 2008, and 2010 were ceftriaxone-sensitive; in contrast in 2009, all (100%) Streptococci-positive isolates were reported to resistant to ceftriaxone. The rates of Streptococci resistance to ciprofloxacin were 20%, 41.67%, 38.09%, and 33.33% in 2007, 2008, 2009, and 2010 respectively. Erythromycin-non-susceptible Streptococci rates decreased from 66.67% in 2007 to 47.62% in 2010.

Enterococci isolated from the entire (100%) specimens were identified to be sensitive to teicoplanin and linezolid and resistant to cloxacillin and oxacillin. The rates of Enterococci sensitivity to vancomycin were 90.91%, 81.25%, 86.67%, and 93.3 in 2007, 2008, 2009, and 2010, respectively. Gentamicin-resistant rates of Enterococci in 2007, 2008, 2009, and 2010 were 25%, 60%, 33.33%, and 66.67%, respectively. Sixty and 66.67% of Enterococci isolates were reported to be amikacin-sensitive in 2007 and 2008; in contrast, all 4 (100%) detected Enterococci in 2010 were resistant to amikacin. Enterococci resistance rates to ampicillin were decreased from 57.14% in 2007 to 14.29% in 2010.

## Discussion

After more than 50 years of clinical use, many antimicrobial agents are not as effective as they used to be (6). Infections caused by resistant microorganisms resulting in prolonged illness, hospital stays, higher costs, and greater risk of death (3). According to Centers for Disease Control and Prevention (CDC) statistics, above 70% of bacteria that cause hospital-acquired infections were resistant to at least 1 of the antibiotics most commonly used to treat them (6). Several studies have demonstrated significant changing trends in the microbiology, epidemiology and clinical as well as predictability of positive cultures over a period of time (7,8). Therefore, periodic surveillances of antimicrobial resistance pattern at national or regional level are vital to patient care and infection prevention.

The highest rate of antimicrobial resistance observed with penicillin G (73.63% to 80.25%) and amoxicillin (33.33% to 80.95%) in the present survey could be partially justified by the fact that according to the result of studying 33,858,186 prescriptions in 2010 in Iran, oral amoxicillin (capsule 500 mg) and intramuscular penicillin (vial 6.3.3) were the third and eighth most commonly prescribed medications, respectively (9). Furthermore, these 2 antibiotics have been available in Iran pharmaceutical market for many years; while, linezolid and teicoplanin are relatively newcomers to the antibiotic front lines.

*S. aureus* was the most frequent gram-positive bacterium isolated from all samples in the current study. It is the most common bacterial pathogen from inpatients and also the second most prevalent one (after *Escherichia coli*) among outpatient isolates in the United States (US) and Latin America (10). Japoni *et al.* reported *S. aureus* as the most pathogenic bacteria (25%) isolated from the 9407 blood samples during a 4 year period in southern Iran (11). The same group identified *S. aureus* as the second most prevalent pathogenic bacteria isolated from 58 patients with nosocomial pneumonia (12). In a 2-year retrospective study at university affiliated hospital in Urmia, northwestern of Iran, coagulase-negative staphylococci (18.7%) and *S. aureus* (18%) were the most common causes of nosocomial bacteraemia (13).

More than three-fifths of *S. aureus* isolates during the (4 year) study period were resistant to penicillin G. *S. aureus* strains were initially susceptible to penicillin G. however, less than 10 years after its introduction to clinical practice, resistance to penicillin G emerged rapidly as a consequence of penicillinase widespread production. Nowadays, most staphylococcal strains are penicillinase producer and virtually resistant to penicillin G (2). In accordance with our results, Rahbar *et al.* reported that 82.6% of *S. aureus* isolated from blood samples of patients at a hospital in northwestern of Iran were resistance to penicillin G (13). In contrast, the resistance of rate of *S. aureus* to penicillin in Dhahira region, Oman was low (39%) (14). Although the authors did not explain the cause of this

phenomenon, decrease in penicillin usage (prescriptions) and implementation of infection control procedures might contribute to the low rate of resistance to penicillins in Oman.

Methicillin introduction into clinical use in 1960 was closely followed by the first reports of methicillin resistant S. aureus (MRSA) through the production of a supplementary penicillin-binding protein (15). The increase in the resistance rate of *S. aureus* to oxacillin from 60.78% to 72% during 4 years in the current study was in congruent with the trends (patterns) reported from other countries. The percentage of MRSA rose from 2.4% in 1975 to 29% in 1991 in the US (16) and increased from 4% in 1990 to 42% in 2000 in England and Wales (17). Rigorous infection control practices set by the government in the United Kingdom (UK) have resulted in the sharp fall in MRSA prevalence from 40-45% during 2001-2005 to 36% in 2007. This is true for most European countries (15). The rate of MRSA reported from several recent studies in Iran ranges from 40% to more than 96% (12,13,18,19).

We found that 1.82% and 3.33% of detected *S. aureus* in 2009 and 2010 were resistant to vancomycin. The first clinical vancomycin-resistant *S. aureus* (VRSA) was isolated from a diabetic foot ulcer in the Michigan, US in 2002 (20). At least 6 more isolates of VRSA have been reported from the US (21). More recently, VRSA have also been reported from India (22). According to the result of a study on 356 *S. aureus* isolates over a period of 1 year in 2005 at an university affiliated hospital in Tehran, 2 (0.56%) strains of *S. aureus* were vancomycin resistant confirmed by minimum inhibitory concentration (MIC) of 64 and 512 mcg/ml for vancomycin as well as detection of vanA gene in 1 of the isolates through polymerase chain reaction (PCR) (23). To our knowledge, VRSA has not been reported from other studies in Iran. The development of VRSA could be attributed to irrational usage and selective pressure of vancomycin (due to fact that vancomycin is the main antimicrobial agent available for the treatment of MRSA infections). Askarian *et al.* demonstrated that for only 12 out of 200 (6%) hospitalized patients in a large university-affiliated hospital in Shiraz, southern Iran, vancomycin was prescribed appropriately according to Healthcare Infection Control Practices Advisory Committee (HICPAC) guidelines (24). Despite considerable concerns, only a very small number of VRSA have been reported so far. Therefore, it seems that VRSA is not a major clinical challenge and is not expected to play a major role in the antimicrobial resistance in the near future (2).

The decreasing pattern of Streptococci resistance to penicillin G during the study period (from 85.71% in 2007 to 62.5% in 2010) is comparable to the US and UK. According to PROTEKT surveillance in the US, the rate of fully resistant *S. pneumoniae* decreased from 26.3% to 16.5% between 2000 and 2004 (25). The prevalence of non-susceptible *S. pneumoniae* isolates from bacteraemia fell from 4.1% in 1999 and 2000 to <2% in 2003-2007 in the UK (15). Kohanteb and Sadeghi reported that 39 out of 115 (33.9%) pneumococcal isolates from Iranian patients with community-acquired pneumococcal infections were penicillin-non-susceptible (MIC > 0.1 mcg/ml)(26). They also observed that 27.8% of penicillin-resistant pneumococcal isolates were also non-susceptible to erythromycin (26). Similar to penicillin G, the rate of Streptococci resistance to erythromycin (a macrolide) declined during the 4 year in our study. In contrast, recent data implicated that despite increasing in high-level macrolide and multidrug resistance, the overall macrolide resistance rates have relatively stabilized in the US (25) and UK (15). Reduced antibiotic usage and introduction of pneumococcal vaccine [23-valent pneumococcal polysaccharide vaccine (PPSV23)] in clinical practice in Iran might be probable causes of declining prevalence of Streptococci resistance to penicillin G and erythromycin.

More than four-fifths Enterococci isolates were susceptible to vancomycin in the present study. Vancomycin-resistant enterococci (VRE) were first demonstrated in the US in 1987 and in the Europe in 1986 (27). According to CDC report, the percentage of (VRE) in nosocomial infections increased from 0.4% to 23.2% among patients in intensive care units and from 0.3% to 15.4% among subjects in noncritical care units during 1989-1997 (28). The LEADER program 2007 identified VRE in 30% of 705 enterococci in the US (29). In most European countries rather than the UK and Ireland, the prevalence of glycopeptide-resistant *E. facium* and *E. fecalis* are below 10% and 5%, respectively. The rate of vancomycin resistance in the UK and Ireland were reported to be 32.1% for *E. facium* and 2.8% for *E. fecalis* (15). Japoni *et al*. identified VRE in 5 from 29 (17.24%) enterococci isolated from blood samples in southern Iran (11). A cross-sectional study during 2 years at a university hospital in Tehran implicated that isolates of 6 from 422 (1.42%) newly admitted patients as well as 7 from 93 (7.52%) patients with either at least 48-hours of hospital stay or chronic

kidney disease under hemodialysis were VRE (30). Several risk factors have been proposed for VRE colonization such as prior use of vancomycin, third-generation cephalosporins, fluoroquinolones, broad-spectrum antibiotics, antibiotics with anaerobes coverage, and prolonged hospitalization (31). The probable risk factors of VRE colonization or infection were not determined in the current survey. Regarding the fact that cefixime and ceftriaxone, third-generation cephalosporins, were among the 10 most frequently prescribed medications in Iran according to the report of National Center of Rational Use Drug in 2008 (32), implementing effective measures in limiting prescription of these antibiotics (apart from other actions such as hand hygiene and decontamination of fomites) could contribute significantly in controlling VRE colonization and subsequent infections.

Susceptibility of all isolated gram-positive bacteria specially enterococci and *S. aureus* to linezolid in the current study is in line with results of most studies from Iran (12,33,34). Linezolid, received FDA approval in 2000, has emerged as an effective treatment option for infections caused by gram-positive bacteria that are resistant to conventional antibacterial agents. Currently, resistance to linezolid remains very uncommon (less than 0.5%) among studied isolates; however, it has been widely reported. The results of the LEADER Program 2008 in the US demonstrated an excellent overall susceptibility rate of 99.64% and only 0.36% of isolated strains were non-susceptible to linezolid (including 3 *S. aureus*, 14 coagulase-negative staphylococci, and 5 *E. facium*). Furthermore, the rate of resistance overall among more 6000 clinical samples was remained stable (35). Nothing that linezolid has not been included in the list of Iranian pharmacopeia yet and is not routinely used in clinical practice except for sporadic, life-threatening cases in which the medication is imported from abroad.

The present survey had several limitations. First, the retrospective methodology of the study did not allow us to compare the results of patients' antibiogram with their clinical condition and response to antimicrobial treatment. Second, determination of antimicrobial susceptibility was performed by the classic disc diffusion rather than other more reliable and accurate methods such as microbroth dilution or E-test. Third, van A and van B genes were not investigated by PCR to confirm isolates suspected to VRSA. Finally, our hospital laboratory was not capable of distinguishing *E. facium* from *E. fecalis* isolates during the study period. Furthermore, the strains of Streptococci (e.g. *S. viridans* and *S. pneumoniae*) were not differentiated in our survey. In conclusion, our data demonstrated that the resistance rate of gram-positive bacteria to common antimicrobial agents such as penicillin G is increasing. In contrast, these microorganisms have been predominantly remained sensitive to antimicrobials with high potency against gram-positives such as vancomycin or relatively-new antimicrobials such as linezolid and teicoplanin. Strategies such as educational programmes for health care professionals, restrictive hospital formulae, active contribution of clinical pharmacists in prescription, administration, and monitoring of antimicrobial agents, development of standard guidelines for treatment of infectious diseases and periodic surveillances of antimicrobial resistance pattern at national or regional level could be substantially effective in reducing the burden of infectious diseases and its clinical as well as economic consequences.

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